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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/796,691	03/08/2004	Marc Bellotti	44378/293531 (13131-0331)	6082

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JOHN S. PRATT, ESQ
KILPATRICK STOCKTON, LLP
1100 PEACHTREE STREET
ATLANTA, GA 30309

EXAMINER	
MONDESI, ROBERT B	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 03/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/796,691	BELLOTTI ET AL.	
	Examiner	Art Unit	
	Robert B. Mondesi	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-24 and 73-82* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4-24 and 73-82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 8, 2006 has been entered.

Information Disclosure Statement

The IDS filed November 9, 2005 has been received and is signed and considered, a copy of the PTO 1449 is attached to the following document.

Status of the Claims

Claims 3, 25-72 have been canceled. **Claims 76-82** are new. **Claims 1-2, 4-24 and 73-82** are presently pending and under examination.

Withdrawal of Objections and Rejections

The objections and rejections not explicitly restated below are withdrawn.

Maintenance of rejections

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

Claims 1-2, 4-24 and 73-75 remain rejected under 35 U.S.C. 102(b) as being anticipated by Clay et al., 1999.

Claims 1-2, 4-24 and 73-75 remain rejected under 35 U.S.C. 102(b) as being anticipated by Durbin et al., 1999.

Double Patenting

Claims 74 and 75 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over **claims 73-78 and 80** of copending Application No. 10996570.

The above rejections were explained in the Office action.

Response to applicant's arguments

In regards to the rejection of **claims 1-2, 4-24 and 73-75** under 35 U.S.C. 102(b) as being anticipated by Clay et al., 1999, applicants assert that the particle derivatives are derived from naturally occurring HDL particles unlike the particles in Clay (as mentioned in Declaration of Mr. Hassibullah Akeefe, filed February 8, 2006).

Applicants assert further that the particle derivatives of the present application are biochemically different from Clay's particles in several aspects such as their lipid composition, for example the reconstituted particles of clay do not contain measurable triaclyglycerol or non-esterified fatty acids, whereas the applicants claimed particle derivatives contain levels of TG comparable to the naturally occurring particles and also contain non-esterified fatty acids (as mentioned in Declaration of Mr. Hassibullah Akeefe, filed February 8, 2006).

Applicants also assert that the particle derivatives of the present application have a different protein composition than that of Clay's, for example in addition to apoA-Al and apo-AII present in Clay's particle derivatives that applicants particle derivative also

contains, "at least one of apolipoprotein C-III, apolipoprotein D or apolipoprotein E", (as mentioned in Declaration of Mr. Hassibullah Akeefe, filed February 8, 2006).

Applicants assert that Clay's particle have apoA-I/apoA-II stochiometirc molar ratios of 1.8 and 2.9, that is an average approximately 2.3 and in contrast applicants' particle derivative inherently posses an apolipoprotein composition similar to the of naturally occurring particles and have an apoA-1/apoA-II stochiometric molar ratio of 3.0 (as mentioned in Declaration of Mr. Hassibullah Akeefe, filed February 8, 2006).

Applicants' arguments have not been found persuasive. On page 455, column, paragraph 2, lines 1-11 to page 456, column 1, lines 1-2, it has been stated that the components of the particle derivatives of Clay were obtained form blood plasma- a natural source. In another words the mentioned components were not produced by recombinant methods or synthesized in a laboratory.

In response to applicants' argument that the references fail to show certain features of applicants' invention, it is noted that the features upon which applicants rely on (i.e., measurable triaclyglycerol or non-esterified fatty acids, at least one of apolipoprotein C-III, apolipoprotein D or apolipoprotein E, an apoA-1/apoA-II stochiometric molar ratio of 3.0) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). However, the examiner notes that some of the mentioned limitations do appear in new **claims 76-82**, present in amendment filed February 8, 2006 (these claims are addressed below under new objections and rejections).

Examiner would like to also point out that all arguments presented by in Declaration of Mr. Hassibullah Akeefe, filed February 8, 2006, were addressed above.

In regards to the rejection of **claims 1-2, 4-24 and 73-75** under 35 U.S.C. 102(b) as being anticipated by Durbin et al., 1999, applicants assert the particles in Durbin are generated using POPC and lipid free apoA-I and lipid free apoA-II, accordingly, the particles in Durbin contain only POPC and cholesterol as their lipid components. Thus, the Durbin particles contain a single phospholipid- POPC. Unlike the Durbin particles, applicants' claimed particle derivative contains phospholipids, comprising at least one phosphatidylcholine (PC), phosphatidyl serine (PS) or phospahatidylethanolamine (PE).

Applicants' arguments have not been found persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., phospholipids, comprising at least one phosphatidylcholine (PC), phosphatidyl serine (PS) or phospahatidylethanolamine (PE)) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In regards to the provisional rejection of the **claims 74 and 75** under the judicially created doctrine of obviousness-type double patenting as being unpatentable over **claims 73-78 and 80** of copending Application No. 10996570, the applicants assert that if the rejection applies when allowable subject matter is found, applicants will address the rejection by filing a terminal disclaimer.

New Objection(s) and Rejection(s)

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2, 4-24 and 73-82 are rejected under 35 U.S.C. 102(e) as being anticipated by Zhu et al., United States Patent Application No. 2004/0106556 in light of applicants own submissions.

The examiner would like to clarify that **claims 1-2, 4-24 and 73-82** are product by process claims and "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)

Zhu et al. disclose delipidated particles comprising high-density lipoproteins (HDL), these particles are prepared by chemically treating plasma containing these

particles. Further, these particles are optionally combined with the patient's blood cells before administration to the patient.

Zhu et. al. teach that the method of the their invention for creating these delipidated particles comprises removing lipid and cholesterol from these particles through a method comprising: obtaining blood containing the lipid, separating the blood cells from the plasma containing lipid, cholesterol and the protein particles and lipoprotein particles, contacting the plasma with a first organic solvent capable of solubilizing the lipid and cholesterol; and, separating a first phase containing the lipids and cholesterol from a second phase wherein the second phase is substantially free of the lipids and cholesterol. Particles in the delipidated plasma fraction may optionally be recombined with the blood cells (Page 1, sections 0009-0011).

Zhu et al. also teach that by the terms "first solvent" or "first organic solvent" "or first extraction solvent" are meant a solvent, comprising one or more solvents, used to facilitate extraction of lipid from a fluid. This solvent will enter the fluid and remain in the fluid until being removed. Suitable first extraction solvents include solvents that extract or dissolve lipid, including but not limited to alcohols, hydrocarbons, amines, ethers, and combinations thereof. First extraction solvents may be combinations of alcohols and ethers. First extraction solvents include, but are not limited to n-butanol, di-isopropyl ether (DIPE), diethyl ether, and combinations thereof (Page 2, paragraph 0033). The term "second extraction solvent" is defined as one or more solvents that facilitate the removal of a portion of the first extraction solvent and extracted lipids. Suitable second extraction solvents include any solvent that facilitates removal of the first extraction

solvent from the fluid. Second extraction solvents include any solvent that facilitates removal of the first extraction solvent including but not limited to ethers, alcohols, hydrocarbons, amines, and combinations thereof. Second extraction solvents include diethyl ether and di-isopropyl ether, which facilitate the removal of alcohols, such as n-butanol, from the fluid. The term "de-emulsifying agent" is a second extraction solvent that assists in the removal of the first solvent and extracted lipids which may be present in an emulsion in an aqueous layer (Page 3, paragraph 0034). In situations where a second extraction solvent is not required to remove a first solvent, the first solvent may be removed through other means including but not limited to pervaporation or activated charcoal. Pervaporation or activated charcoal may also be employed to remove second extraction solvents (Page 3, paragraph 0035).

Zhu et al. teach further that it is an object of their invention to provide at least partially delipidated protein and lipoprotein particles that are associated with lipid transport or metabolism comprising one or more of at least partially delipidated HDL, LDL, and VLDL particles (Page 2, section 0014).

Zhu et al. also teach that by the term "fluid" is meant any fluid, including but not limited to, a biological fluid obtained from an organism such as an animal or human. Such biological fluids obtained from an organism include but are not limited to blood, plasma, serum, cerebrospinal fluid, lymphatic fluid, peritoneal fluid, and any other fluid contained within the organism. Blood provides the plasma and serum to be treated with the method of the present invention (Page 2, section 0032).

Zhu et al. teach further that the term "lipid" is defined as any one or more of a group of fats or fat-like substances occurring in humans or animals. The fats or fat-like substances are characterized by their insolubility in water and solubility in organic solvents. The term "lipid" is known to those of ordinary skill in the art and includes, but is not limited to, complex lipid, simple lipid, triglycerides, fatty acids, glycerophospholipids (phospholipids), true fats such as esters of fatty acids, glycerol, cerebrosides, waxes, and sterols such as cholesterol and ergosterol (Page 3, section 0036) and that he term "delipidation" refers to the process of removing at least a portion of a total concentration of lipids in a fluid such as plasma and serum. Plasma and serum are used interchangeably herein. The term "delipidation" also refers to removal of lipid from any protein particle or lipoprotein particle capable of binding lipid (Page 3, section 0036).

Zhu et al. teach that by the term "particle" is meant any particle found in a biological fluid, particularly blood, plasma and serum, that is associated in some way with lipid transport or metabolism. Such particles include protein and lipoprotein particles and are known to one of skill in the art. Such particles include, but are not limited to, HDL, LDL and VLDL. These particles are chemically modified to partially or substantially reduce their lipid content, thereby creating delipidated particles (Page 3, section 0040).

Zhu et al. also teach that after contacting the fluid containing the lipid with the first solvent as described above, the first solvent and fluid are mixed, using methods

including but not limited to one of the following suitable mixing methods: gentle stirring; vigorous stirring; vortexing; swirling; homogenization; and, end-over-end rotation (Page 5, paragraph 0065) and that Static mixing methods in static mixing tubes may also be employed (Page 5, paragraph 006, lines 18-20) and that biological fluid, for example, blood, is removed from an animal or a human through means known to one of ordinary skill in the art, such as a catheter (Page 6, paragraph 0075, lines 2-4).

Finally and most importantly, Zhu et al. teach that the data from two pigs is shown in Table 1. and the data indicate that the delipidation procedure dramatically reduced TC, TG, cholesterol associated with HDL, and cholesterol associated with LDL in the plasma samples (referred to as post delipidation/post charcoal plasma). Following infusion into individual pigs (indicated as # 1 or #2) of this delipidated sample containing the HDL and LDL particles with greatly reduced cholesterol, the levels of TC, TG, cholesterol associated with HDL, and cholesterol associated with LDL in the plasma were reduced (compare pig #1 pre- vs post-infusion and pig #2 pre- vs post-infusion). Taken together, these data indicate that the delipidation procedure and administration of the delipidated sample containing delipidated HDL and LDL particles is effective in reducing the levels of cholesterol, lipids and lipoproteins involved in lipid transport and metabolism (Page 9, section 0107).

It is important to point out that the applicants have submitted on the record that particle derivatives comprising HDL obtained from a natural source inherently retain similar composition and distribution of apolipoproteins to those found in biological fluids, in particular in addition to apoA-I and apo-AII the mentioned particle derivatives

comprise at least one of apoC-III, apoD or apoE (Page 13, paragraph 1, lines 2-6 of response section of amendment filed February 8, 2006 and page 3, section 6, lines 2-5, of Declaration filed by Hassibullah Akeefe on February 8, 2006).

Thus Zhu et al. teach all the elements of **claims 1-2, 4-24 and 73-82** and these claims are anticipated under 35 USC 102(e).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 75 and 80-82 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over **claims 73- 78, 80 and 85-90** of copending Application No. 10996570. Although the conflicting claims are not identical, they are not patentably distinct from each other because **claims 80-82** are further limitations of **claim 75** that state: the composition of the claimed invention further

comprises at least one of apolipoprotein C-III, apolipoprotein D, apolipoprotein E, triglycerides, or fatty acids. As previously indicated in Office action mailed September 9, 2005, **claim 75** of the present application discloses an obvious variant of the composition taught by **claims 73-78 and 80** of Application No. 10996570. The newly added **claims 85-90** in amendment filed February 8, 2006 of Application 10996570 presently teach that the composition of the claimed invention further comprises at least one of apolipoprotein C-III, apolipoprotein D, apolipoprotein E, triglycerides, or fatty acids.

Claims 1, 8, 13 and 76-79 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over **claims 91-93** of copending Application No. 10996570. Although the conflicting claims are not identical, they are not patentably distinct from each other because **claims 1, 8, 13 and 76-79** of the present application disclose a composition comprising a HDL particle derivative wherein the particle derivative comprises apolipoprotein A-I and phospholipids wherein the lipid content or the cholesterol content of the composition has been lowered and wherein the composition further comprises at least one of apolipoprotein C-III, apolipoprotein D, apolipoprotein E, triglycerides, or fatty acids. Consequently **claims 91-93** of application 10996570 also disclose a composition comprising a HDL particle derivative wherein the particle derivative comprises apolipoprotein A-I, and phospholipids wherein the lipid content or the cholesterol content of the composition has been lowered and wherein the composition further

comprises at least one of apolipoprotein C-III, apolipoprotein D, apolipoprotein E, triglycerides, or fatty acids.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert B. Mondesi
Patent Examiner
Group 1653
Robert B. Mon
3-27-06

JON WEBER
SUPERVISORY PATENT EXAMINER